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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/458,580

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MILES B. BRENNAN

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02/26/2003

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EXAMINER

ZITOMER, STEPHANIE W

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 02/26/2003

22

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/458,580

Applicant(s)

BRENNAN ET AL.

Examiner

Stephanie Zitomer

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 December 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 4, 5, 7, 9, 10, 13, 16, 18-21, 23-29, 31-39, 53-56, 59, 98, 99, 102, 103, 117 and 119 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 20. 6) ☐ Other: _____

Continuation of Disposition of Claims: Claims pending in the application are 1,4-7,9,10,13,16,18-21,23-29,31-39,53-56,59,66-68,70,73,75,80-82,85-91,93-95,98-100,108-114 and 116-119.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 6,66-68,70,73,75,80-82,85-91,93-95,100,108-114,116 and 118.

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DETAILED ACTION

Application status

1. Receipt of the Amendment and Response filed December 2, 2002 is acknowledged.
2. Objections and rejections not reiterated herein from the previous Office action, paper no. 17, mailed October 8, 2002, have been withdrawn in view of amendments to the claims.
3. The previous indication in paper no. 17 of allowability of claims is withdrawn in view of new grounds for rejection.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections under 35 U.S.C. 112, second paragraph: Indefiniteness

4. Claims 1, 4, 5, 7, 9, 10, 13, 16, 18-21, 23-29, 31-39, 53-56, 59, 98, 99, 102, 103, 117 and 119 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention

(a) Claims 1 and claims dependent therefrom other than claim 4 and claim 59 are confusing in containing non-elected subject matter wherein the compound group includes "an α -MSH agonist". The definition of "agonist compound" at page 32 of the specification, lines 26-27, states that the phrase refers to a "mimetic (peptide or nonpeptide) of a POMC peptide". Although the first paragraph of paper no. 17 acknowledges "an α -MSH agonist" as a member of the group from which the compound is selected, the paragraph also states that mimetics are excluded. This is because the elected compound species includes only those amino acid sequences that are structurally related to α -MSH. Mimetics, especially nonpeptide mimetics, are not structurally related to α -MSH and may not even contain amino acids. Claim 1 may be amended to recite that the "agonist" is a --homologue of α -MSH having agonist activity-- as in claim 4.

(b) Claim 1 and claims dependent therefrom are confusing due to the typographical error in line 6 at "eight" which should be --weight--.

(c) Claim 1 and claims dependent therefrom are confusing because the phrase "represented by" renders the claims indefinite in that the claims include elements not actually disclosed (those encompassed by "represented"), thereby rendering the scope of the claims unascertainable. See MPEP § 2173.05(d). See especially claims 1, 7 and 9. It is suggested to amend claim by deleting "sequences represented by" and to amend claims 7 and 9 by deleting "represented herein by" and "represented by", respectively and changing "an" before "amino" to --the--.

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(d) Claims 1 and claims dependent therefrom are confusing due to missing the word "sequence" after "amino acid" in lines 9-10.

(e) Claim 4 is confusing in containing the nonelected subject matter, "a non peptide mimetic of α -MSH having α -MSH agonist activity". It is suggested to delete the nonelected material.

(f) Claims 18, 31 and 39 are confusing due to typographical errors. In claim 18, "Linder" should be --under--. In claim 31, "cart" should be --can--. In claim 39, the "d" before "leptin" and " μ pg" are not understood.

(g) In claim 59 the term "substantially" is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is suggested to point out a definition in the specification or to delete the term.

(h) Claims 117 and 119 are confusing in containing nonelected subject matter. It is suggested to cancel claim 117 and delete (b)-(k) in claim 119.

Rejection under 35 U.S.C. 102(b): Anticipation

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 4, 7, 9, 10, 19-21, 23-27, 31, 53, 59, 98 and 99 are rejected under 35 U.S.C. 102(b) as being anticipated by the patent to Girtten et al. (5,726,156) with Mountjoy et al. 1997 (Mol. Cell. Endocrinol. 128:171-177).

The method of claims 1, 4, 7 and 9 comprising administering to the periphery of an animal a therapeutic composition comprising an MSH compound which is an α -MSH analog in an amount effective to measurably decrease body weight or reduce the rate of weight gain compared to that in the absence of said administering wherein the compound is an analog of a peptide represented by SEQ ID NO:1 or 2 is disclosed at column 28, Example XX with column 16, Example II. Therapeutic compositions are disclosed at column 7, line 64-column 8, line 17.

Regarding claim 10, the α -MSH compound in the method of claim 1 inherently has the identifying characteristics recited in claim 10, i.e., ability to bind MCR expressed in peripheral

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tissues and stimulating lipolysis because these properties of α -MSH were known in the prior art (for example, Mountjoy et al., page 173, first full paragraph; page 175 at 3.).

Regarding claims 19-21 and 23, Girtten et al. disclose transdermal, topical, parenteral and controlled release (skin patch) administration of the α -MSH analog of claim 1 (column 13, lines 28-42).

Regarding claim 24, Girtten et al. disclose that administration of the α -MSH analog of claim 1 was insufficient to cause a statistically significant change in the appetite of the animal as compared to before administration of the analog (column 28, lines 53-55).

Regarding claims 25-27, Girtten et al. disclose administration of the α -MSH analog of claim 1 in ranged amounts overlapping those of the claims (column 14, lines 7-12: about 0.0001 to 0.5 or to 100 mg/kg body weight depending on route of administration; column 28, Example XX).

Regarding claim 31, Girtten et al. disclose that the decrease in body weight can be measured within at least about one week of administration of the α -MSH analog (column 28, lines 49-55).

Regarding claim 53, Girtten et al. disclose the method of claim 1 wherein the animal is a human (column 2, line 65-column 3, line 1; column 9, lines 31-35).

Regarding claim 59, the claimed method comprising administering to an animal an α -MSH agonist in an amount effective to bind to melanocortin receptors in peripheral tissues, said effective amount (a) being insufficient to substantially change the appetite; (b) being between 0.1 μ and 10 mg per kg of body weight; (c) being sufficient to affect lipolysis or fatty acids uptake by adipocytes; and (d) being effective to measurably decrease body weight or reduce the rate of weight gain is disclosed by Girtten et al at column 28, Example XX wherein binding of α -MSH agonists to melanocortin receptors was known in the prior art (for example, Mountjoy et al., abstract).

Regarding claims 98 and 99, Girtten et al. disclose the method of claim 1 wherein the animal is at risk for or suffering from an obesity associated disorder including NIDDM (column 11, lines 49-63) and cardiovascular disease (column 12, lines 10-20).

Rejections under 35 U.S.C 103(a): Obviousness

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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6. Claims 13, 16, 18 and 54-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Girtten et al. (56,726,156) as applied to claim 1 above, and further in view of Mountjoy et al. 1997 (Mol. Cell. Endocrinol. 128:171-177) and Hadley et al. (5,731,408). The claim 13 embodiment of the claim 1 method differs from the method of Girtten et al. wherein the MSH compound is α -MSH. However, it would have been obvious and the skilled practitioner in the art would have been motivated at the time the claimed invention was made to use the native MSH compound for the obvious benefit of convenience in obviating chemical synthesis of analogs and in view of its known functions on which the Girtten et al. method depends.

The embodiments of the claim 1 method in claims 16 and 18 differ from the Girtten et al. method wherein the MSH compound binds with higher affinity to a receptor in peripheral tissues than it does to MC4-R receptors and wherein the compound does not activate MC4-R. However, Mountjoy et al. teach that MC4-R receptors occur primarily in the brain (page 172, column 2, lines 5-7) rather than in peripheral tissues whereas a different receptor, MC5-R, occurs in adipocytes and other peripheral tissues (page 172, Table 1; page 175 at 3.). Therefore, it would have been obvious and the skilled practitioner in the art would have been motivated at the time the claimed invention was made to improve on the weight-reducing method of Girtten et al. by making it more specific for fat loss via directing the MSH compound to receptors in adipose tissue while minimizing side effects of binding to MC4-R receptors in the brain.

Regarding claims 54-56, the method of Girtten et al. differs from that of claim 1 wherein the therapeutic composition further comprises an antagonist of MC4-R or an agent that inhibits binding of the MSH compound to MC4-R or inhibits it from entering the central nervous system. However, Hadley et al. teach antagonists of MC4-R which may be used to block the physiological response of cells to α -MSH (column 6, Table III; lines 48-50). It would have been obvious and the skilled practitioner in the art would have been motivated at the time the claimed invention was made to improve on the weight-reducing method of Girtten et al. by making it more specific for fat loss by including with the α -MSH compound an antagonist of MC4-R or an agent that inhibits binding of the MSH compound to MC4-R or inhibits it from entering the central nervous system such as the peptides taught by Hadley et al. for the obvious benefit of by making the method more specific for fat loss via minimizing binding to MC4-R receptors in the central nervous system.

7. Claims 28, 29 and 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Girtten et al. (56,726,156) as applied to claim 1 above and further in view of routine art practice. The claimed embodiments of the claim 1 method differ from the Girtten et al. method wherein ranges for the concentration of the MSH compound in the therapeutic composition are specified

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whereas the reference provides the dose ranges of the MSH compound (column 14, lines 7-12). However, in view of routine practice in the art and absent unexpected results, it would have been obvious and the skilled practitioner in the art would have been motivated at the time the claimed invention was made to determine the concentration of the MSH compound in the composition based on experimental parameters and expected results. In *In re Aller*, 105 USPQ 233, the court found that changes of an old process within the broad teaching of the prior art does not impart patentability in the absence of unexpected results.

The embodiments of the claim 1 method of claims 32-34 differ from the method of Girten et al. wherein serum MSH and leptin levels and ratio are measured prior to administration of the MSH compound. However, in view of routine practice in the art and absent unexpected results, it would have been obvious and the skilled practitioner in the art would have been motivated at the time the claimed invention was made to determine the levels and ratio of MSH and leptin in serum prior to therapy for the obvious benefit of obtaining a baseline measurement from which to determine appropriate therapeutic amounts of the MSH compound to be administered and from which to measure serum levels of administered compound in view of the known role of leptin in weight loss. In *In re Aller*, 105 USPQ 233, the court found that changes of an old process within the broad teaching of the prior art does not impart patentability in the absence of unexpected results.

Regarding claim 35, it would have been further obvious in view of art practice and one of ordinary skill in the art at the time the claimed invention was made would have been motivated to determine the BMI of an individual for the obvious benefit of establishing a baseline weight prior to treatment from which to measure weight loss.

8. Claims 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Girten et al. (56,726,156) as applied to claim 1 above, and further in view of Mountjoy et al. 1997 (Mol. Cell. Endocrinol. 128:171-177). The embodiments of claims 36-39 of the method of claim 1 differ from the method of Girten et al. wherein the therapeutic composition further comprises another body weight regulating agent; wherein the agent is leptin; wherein the ratio of MSH compound to leptin is about 1:100; and wherein the leptin dose is about 0.1 µg to about 100 mg per kg body weight of the animal. However, Mountjoy et al. teach that leptin is produced by fat and when administered to mice causes them to lose weight by decreasing their food intake (page 174 at 7., lines 6-9). It would have been obvious and the skilled practitioner in the art would have been motivated at the time the claimed invention was made to add another body weight regulating agent, especially leptin, to the MSH compound administered in the method of Girten et al. in view of the further teaching of

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Mountjoy et al. that α -MSH increases lipolysis and may regulate leptin production indirectly by decreasing adipose tissue mass (page 174, column 2, lines 15-19) for the obvious benefit of increasing the potential for weight loss via fat reduction. Furthermore, the Court stated, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

9. Claims 102 and 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Girten et al. (56,726,156) as applied to claim 1 above, and further in view of scientific reasoning. The claim 102-103 embodiments of the claim 1 therapeutic method differ from the method of Girten et al. wherein the body weight to be decreased is a side effect resulting from administration of a pharmaceutical compound wherein the pharmaceutical compound is selected from valproic acid, lithium et al.. However, absent evidence to the contrary, it would have been known to the skilled practitioner in the art at the time the claimed invention was made that the cause of the body weight to be reduced was immaterial to the practice of the claimed invention therapeutic method. Therefore, the Girten et al. method would have been the same as the method of claim 1 in the embodiments of claims 102 and 103.

10. Claim 119 is rejected under 35 U.S.C. 103(a) as being unpatentable over Girten et al. (56,726,156) as applied to claim 1 above, and further in view of Hraby et al. (4,485,039 and 5,714,576). The claim 1 method embodiment of claim 119 differs from that of Girten et al. wherein the α -MSH analog is Ac-[Cys⁴, D-Phe⁷, Cys¹⁰] α -MSH wherein the Cys residues are connected by a disulfide bond. However, Girten et al. teach cyclic α -MSH analog peptides which may be produced by inducing the formation of a covalent bond between two reactive amino acid side chains wherein "[o]ne skilled in the art would know that the choice of a particular cyclic peptide is determined by the reactive groups present on the peptide as well as the desired characteristics of the peptide" (column 7, lines 37-54). Hraby et al. '576 teach Ac-[Cys⁴, D-Phe⁷, Cys¹⁰] α -MSH in which the Cys residues are connected by a covalent bond (column 4, line ~27). It would have been obvious and the skilled practitioner in the art would have been motivated at the time the claimed invention was made to substitute an α -MSH analog peptide such as the Ac-[Cys⁴, D-Phe⁷, Cys¹⁰] α -MSH analog of Hraby '576 for the α -MSH analog in the therapeutic method of Girten et al. in view of the teaching of Girten et al. that "a cyclic peptide may provide...increased stability, increased solubility, decreased immunogenicity or decreased clearance in vivo" (column 7, lines 51-54) and the teaching of Hraby et al. '039 that α -MSH has an extremely short half-life in

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serum whereas the α -MSH analogs having Cys⁴ and Cys¹⁰ substitutions and connected by a covalent bond exhibit prolonged biological activity and greater resistance to enzymatic degradation than the native peptide (column 2, lines 57-64; column 3, lines 18-24) as well as the teaching of Hruby et al. '576 that substitution of D-Phe for Phe at position 7 of the Hruby et al. '039 peptide resulted in enhanced and prolonged activity (column 3, lines 1-3).

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 9:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724. The examiner's Rightfax number is 703-746-3148.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196. For questions and requests relating to formal matters contact LIE Chantae Dessau at 703-605-1237.



Stephanie Zitomer, Ph.D.
February 24, 2003

**STEPHANIE W. ZITOMER
PRIMARY EXAMINER**